

# Connectomics and Graph Theory

Jon Clayden <[j.clayden@ucl.ac.uk](mailto:j.clayden@ucl.ac.uk)>

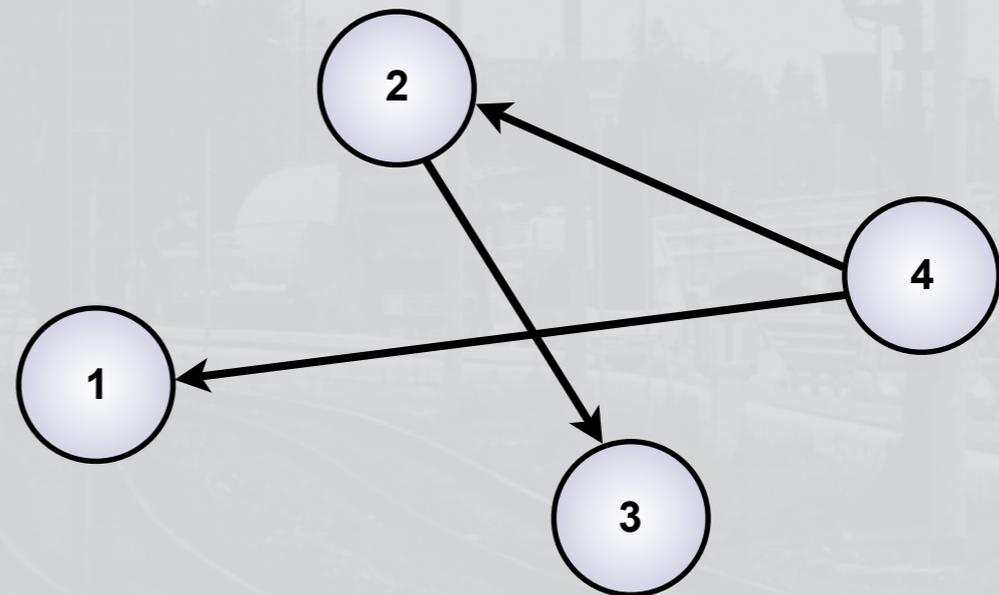
DIBS Teaching Seminar, 20 Nov 2015

## Overview

- What is a graph?
- Real problems as graph problems
- Graphs in neuroscience and neuroimaging
- Representing brain connectivity using graphs
- Advantages and limitations of this approach
- Robustness of *in vivo* connectomes
- The importance of subnetworks
- Combining information from multiple modalities
- Future work

# Graphs

- A highly abstract representation of a set of **vertices** connected by **edges**
- Edges may be **directed** or **undirected**, and may have associated **weights** or costs
- A natural representation of connected systems
- Theoretically very well characterised
- Broad range of applications



# The bridges of Königsberg

- Vertices are **pieces of land**; edges are **bridges**
- Can you walk around the town crossing every bridge once?
- Note: multiple links between two vertices make this a “multigraph”

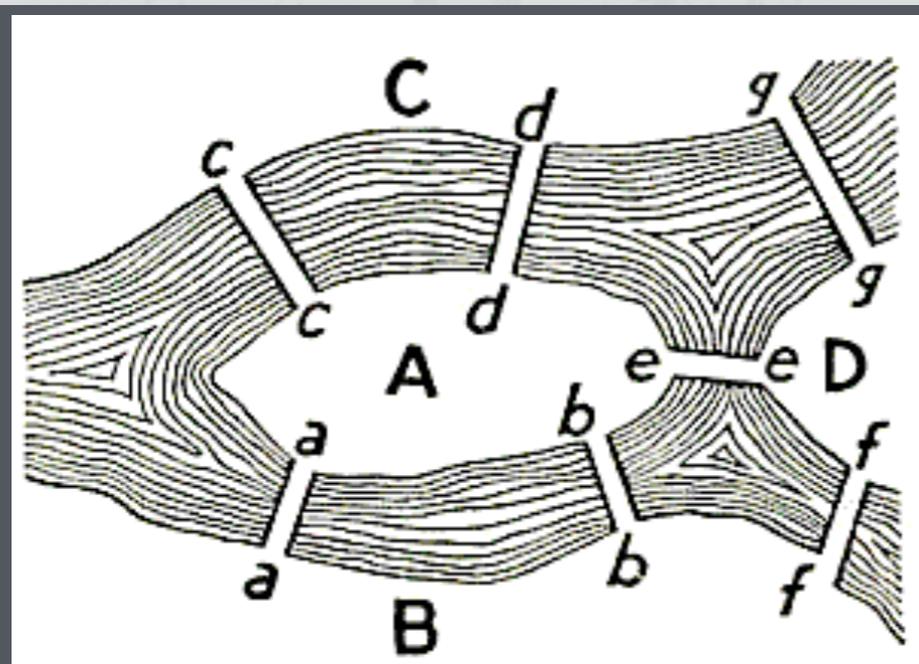
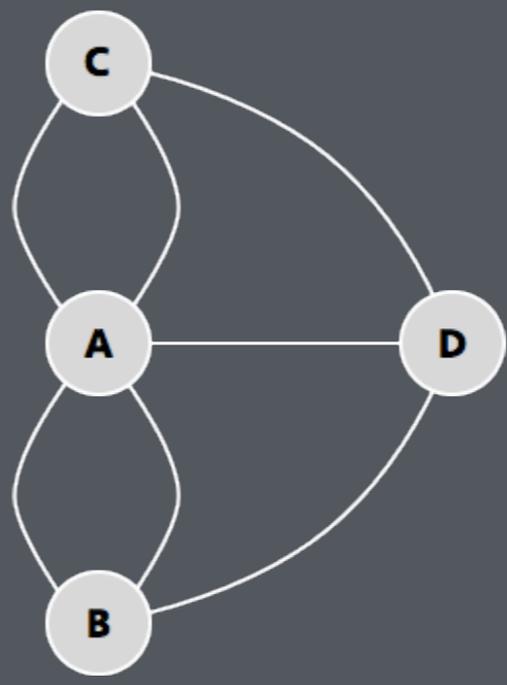


FIGURE 98. *Geographic Map: The Königsberg Bridges.*

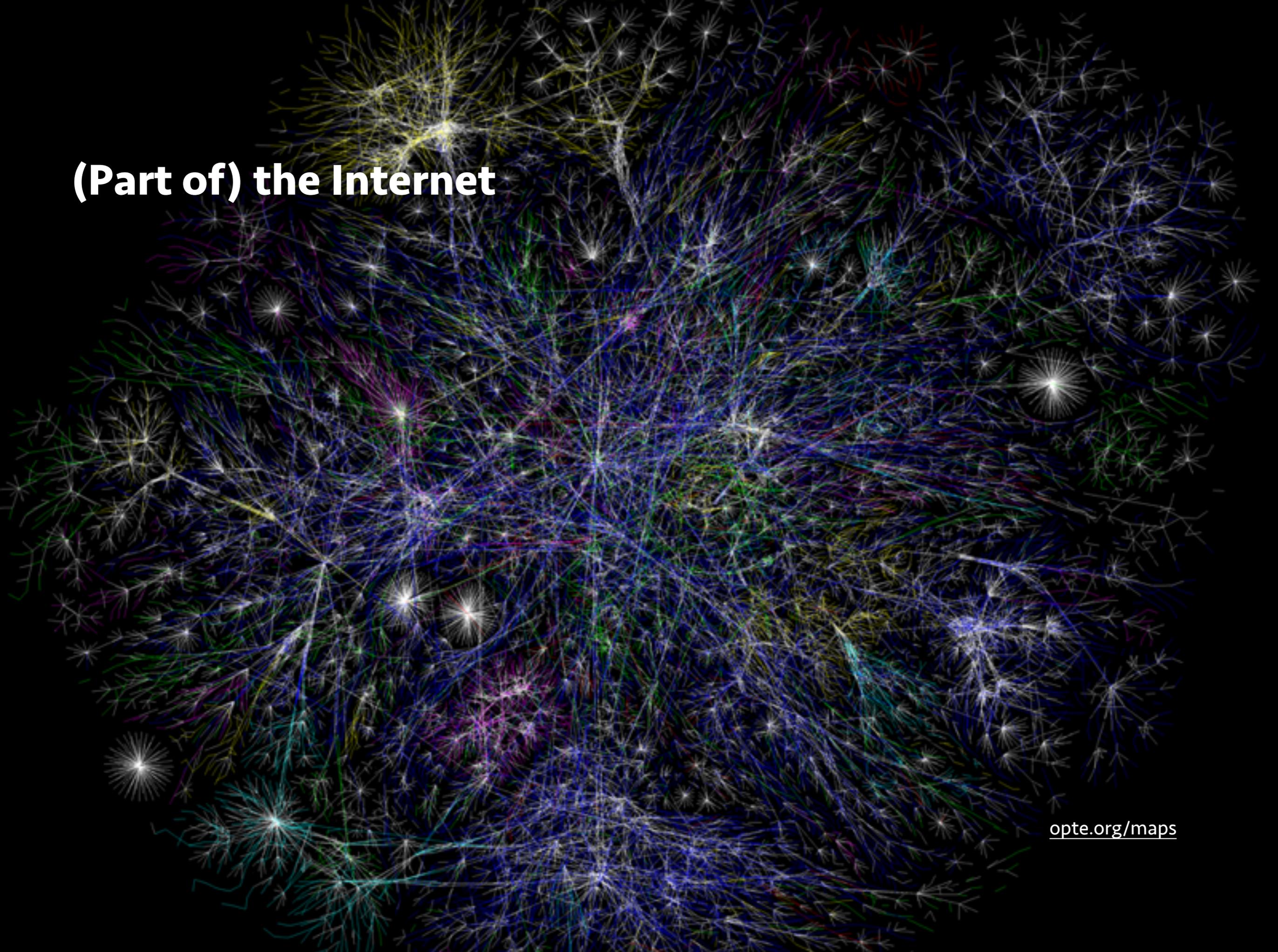


# A more modern graph problem

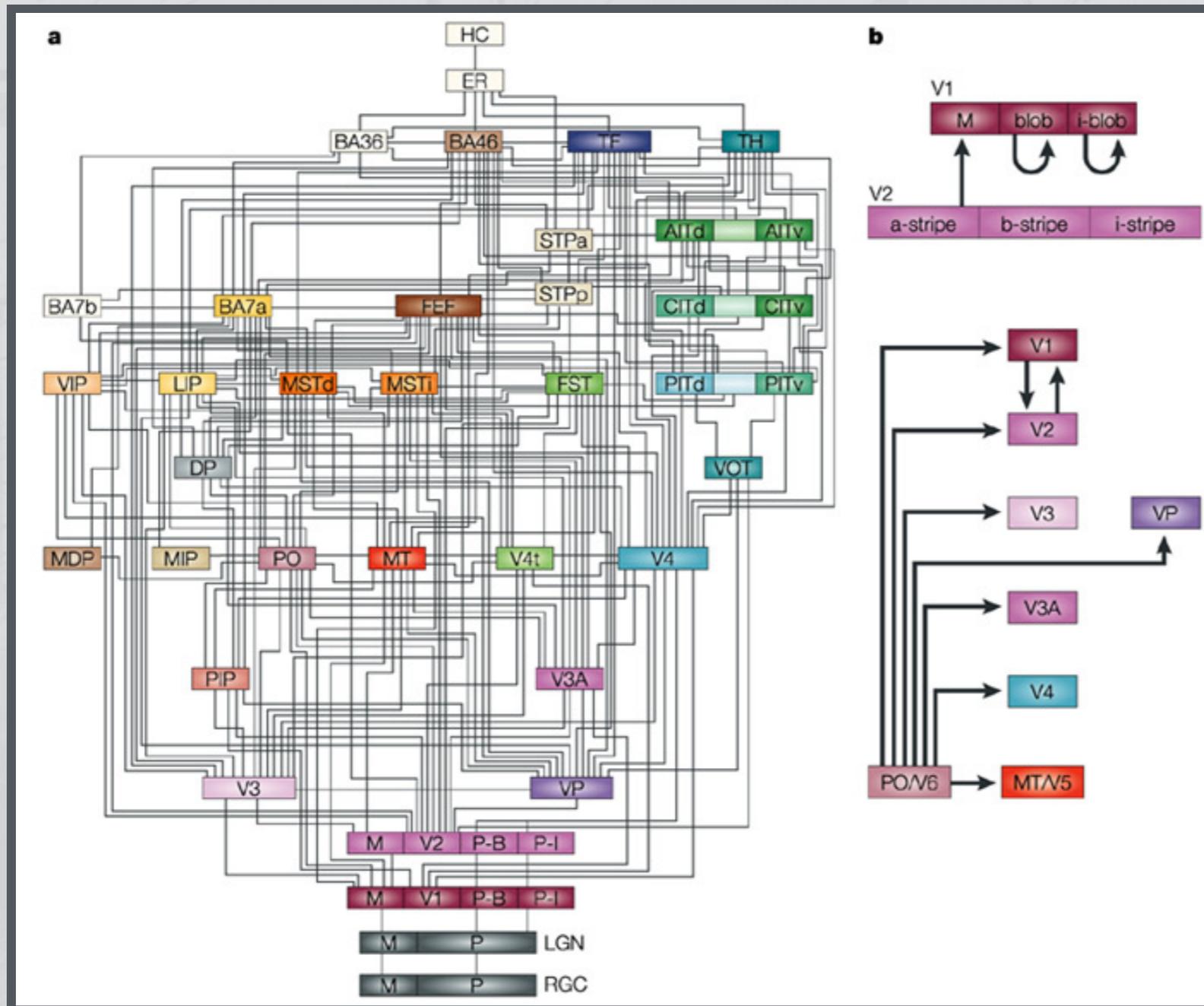


- Travel times as edge costs

# **(Part of) the Internet**

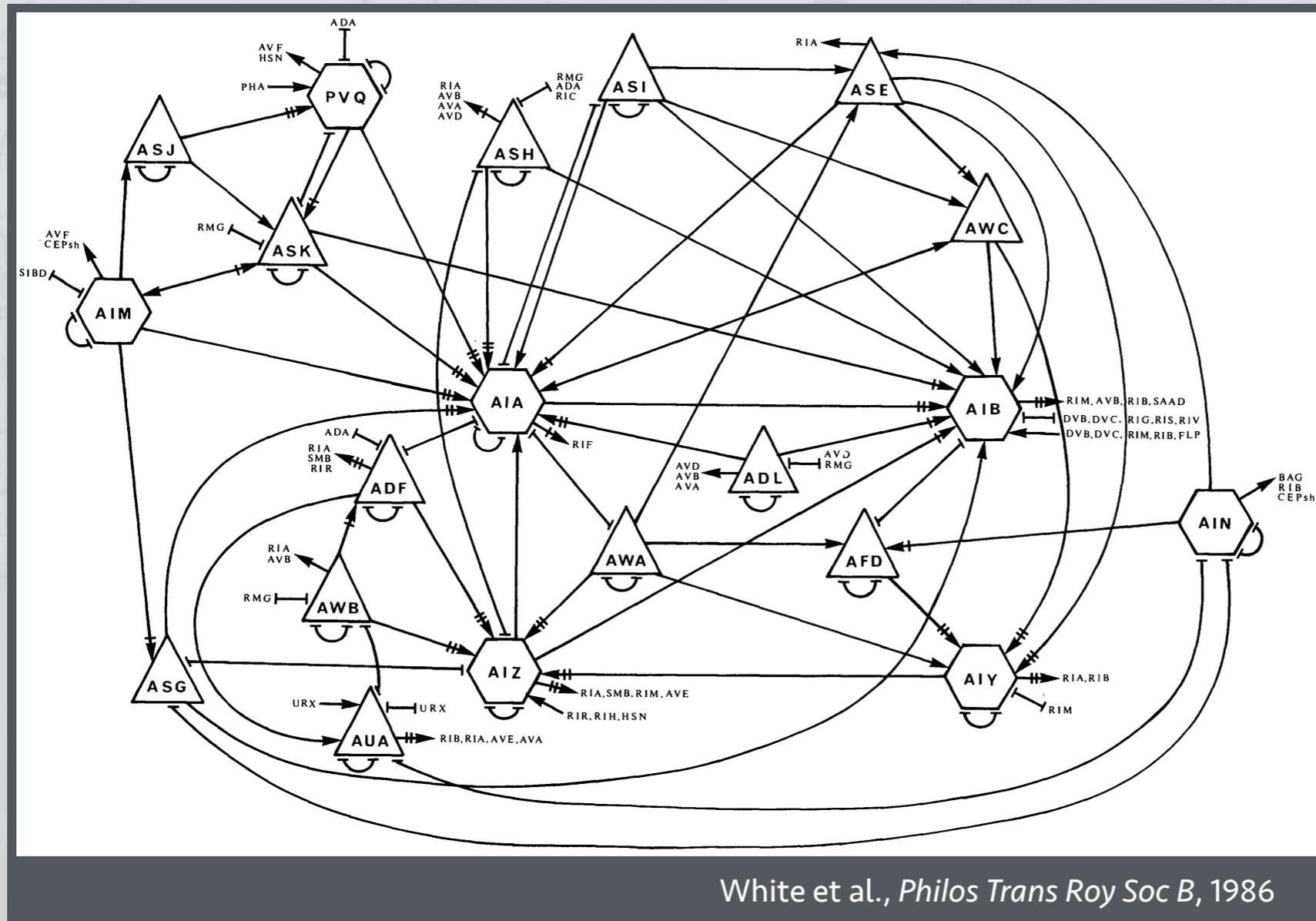


# Connectivity and the brain



Rees et al., *Nat Rev Neurosci*, 2002  
 (after Felleman & van Essen, *Cereb Cortex*, 1991)

# The "connectome"



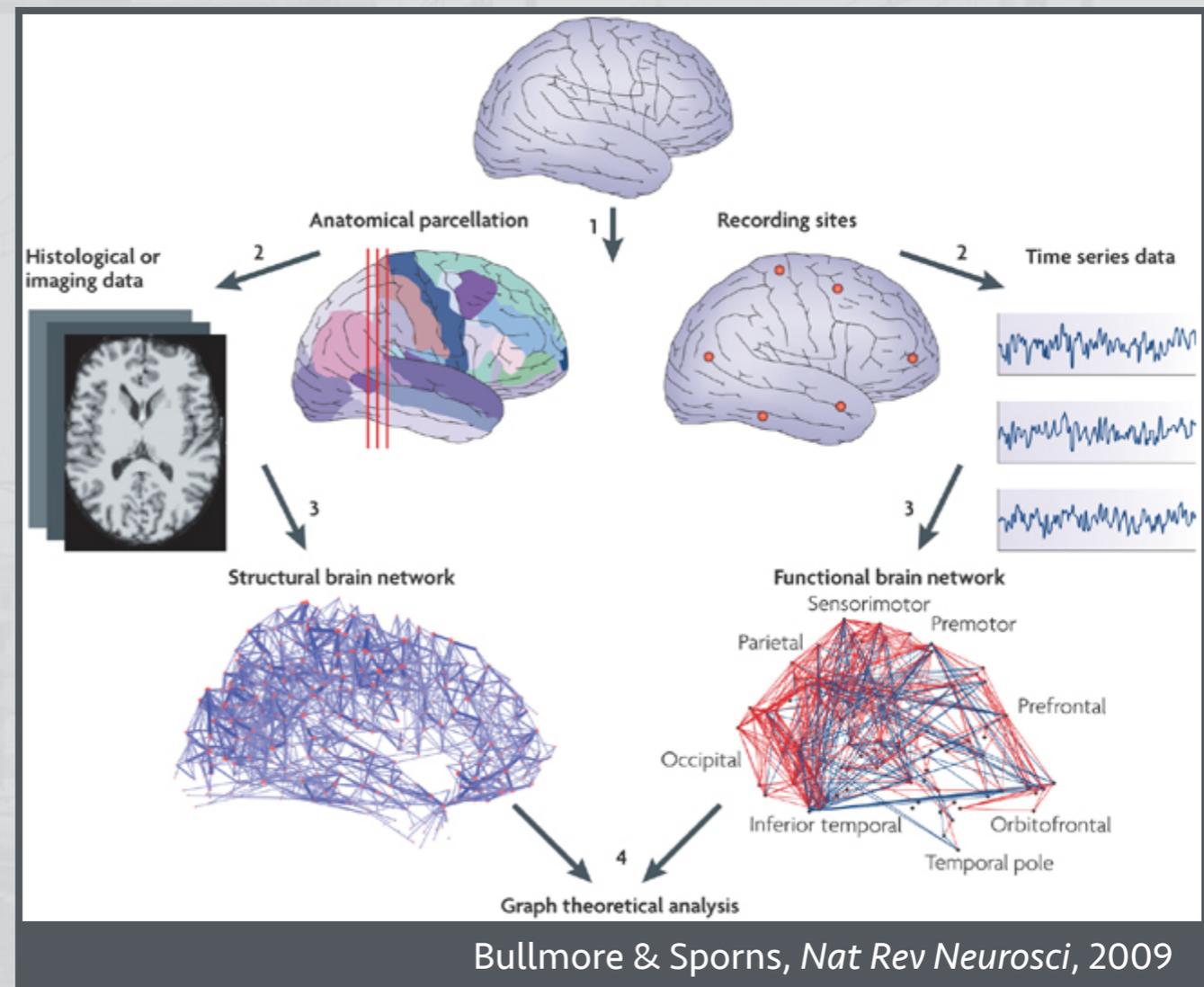
- Circuitry of the nematode nervous system is fully mapped out

## Connection and disconnection

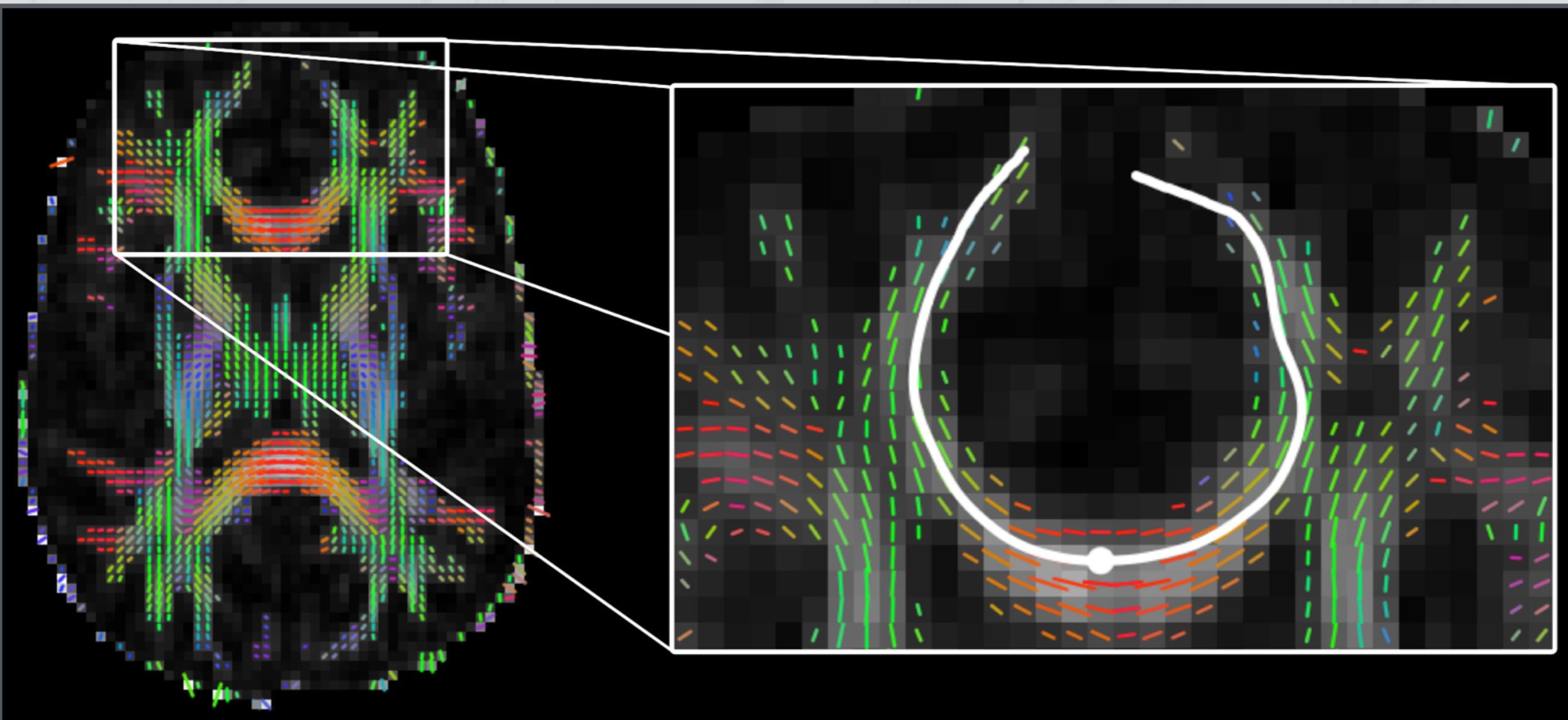
- Development of the brain's connectivity continues for years after birth
- Differences in connectivity patterns may underlie some of the variability in **intelligence** and cognitive **information processing**
- Disconnection between brain regions thought to be a key factor in age-related cognitive decline
- Many neurological diseases are also thought to be associated with loss of connectivity (**disconnection syndromes**)
- Preserving connectivity is extremely important to ensure an optimal outcome after brain surgery
- **Neuroimaging** offers the chance to study connectivity *in vivo*
- Information can come from structural or functional MRI, EEG, MEG, etc.

## Definitions of connectivity

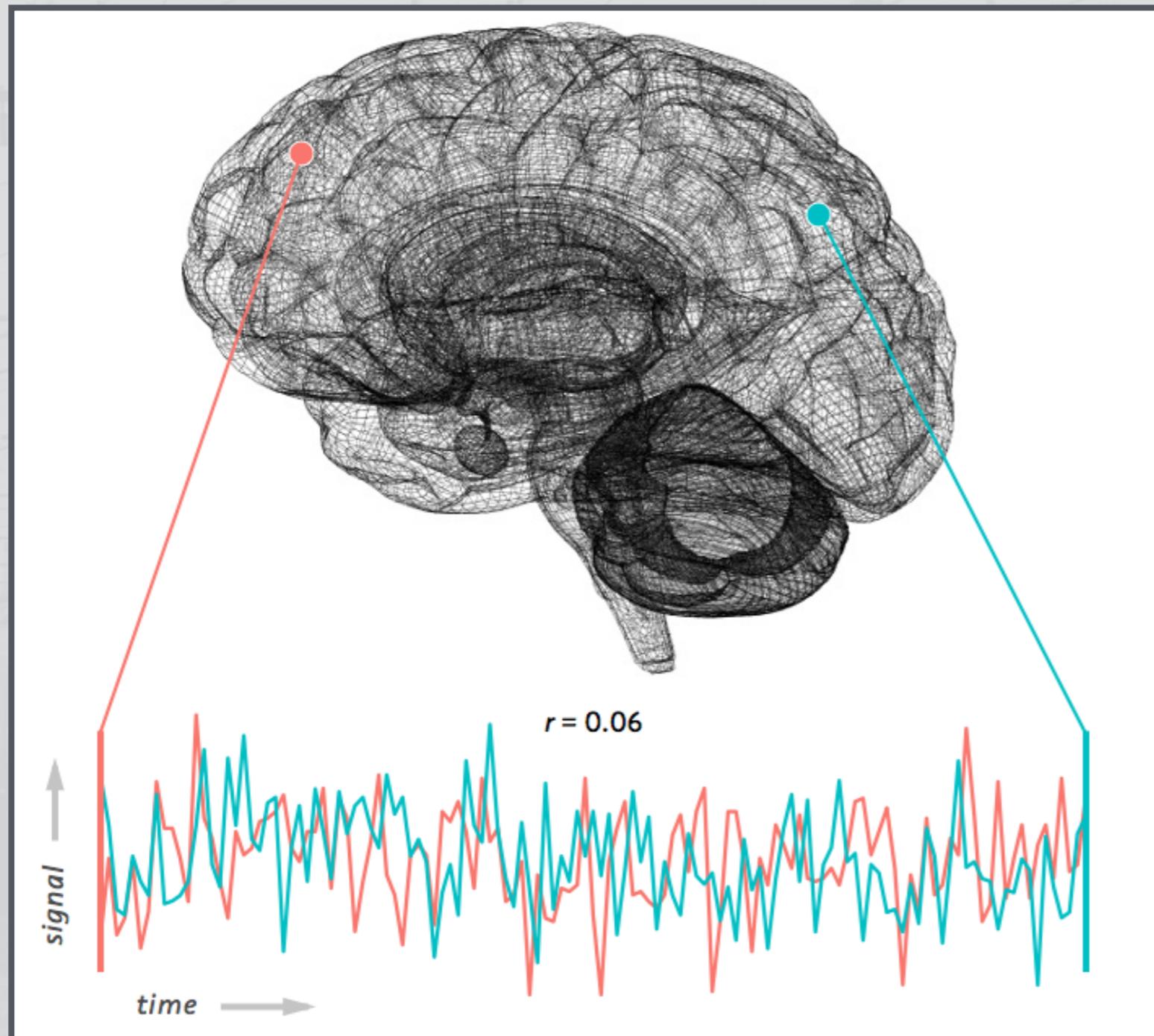
- **Structural connectivity:**  
the physical axon bundles connecting brain regions together
- **Functional connectivity:**  
associations between neural activity in spatially remote regions of grey matter
- **Effective connectivity:**  
patterns of influence by some neural systems over others



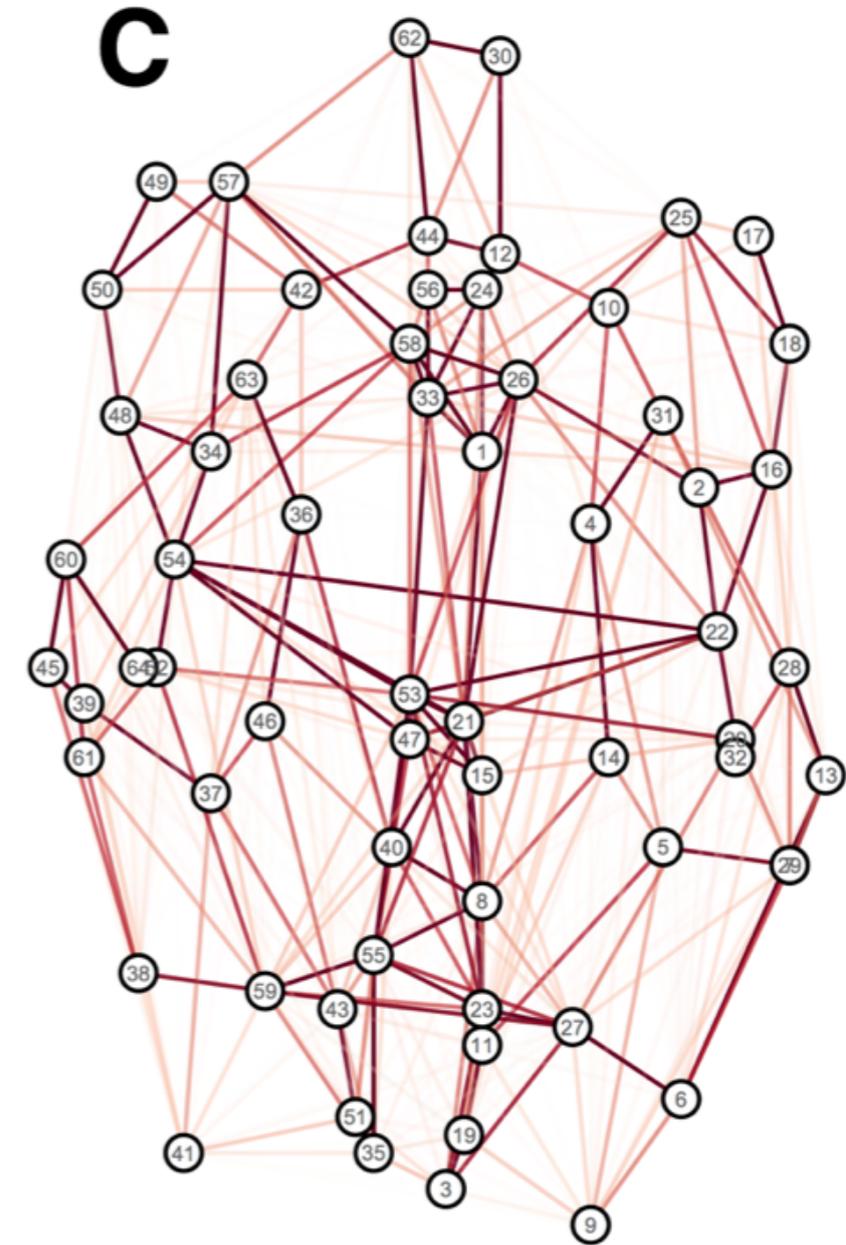
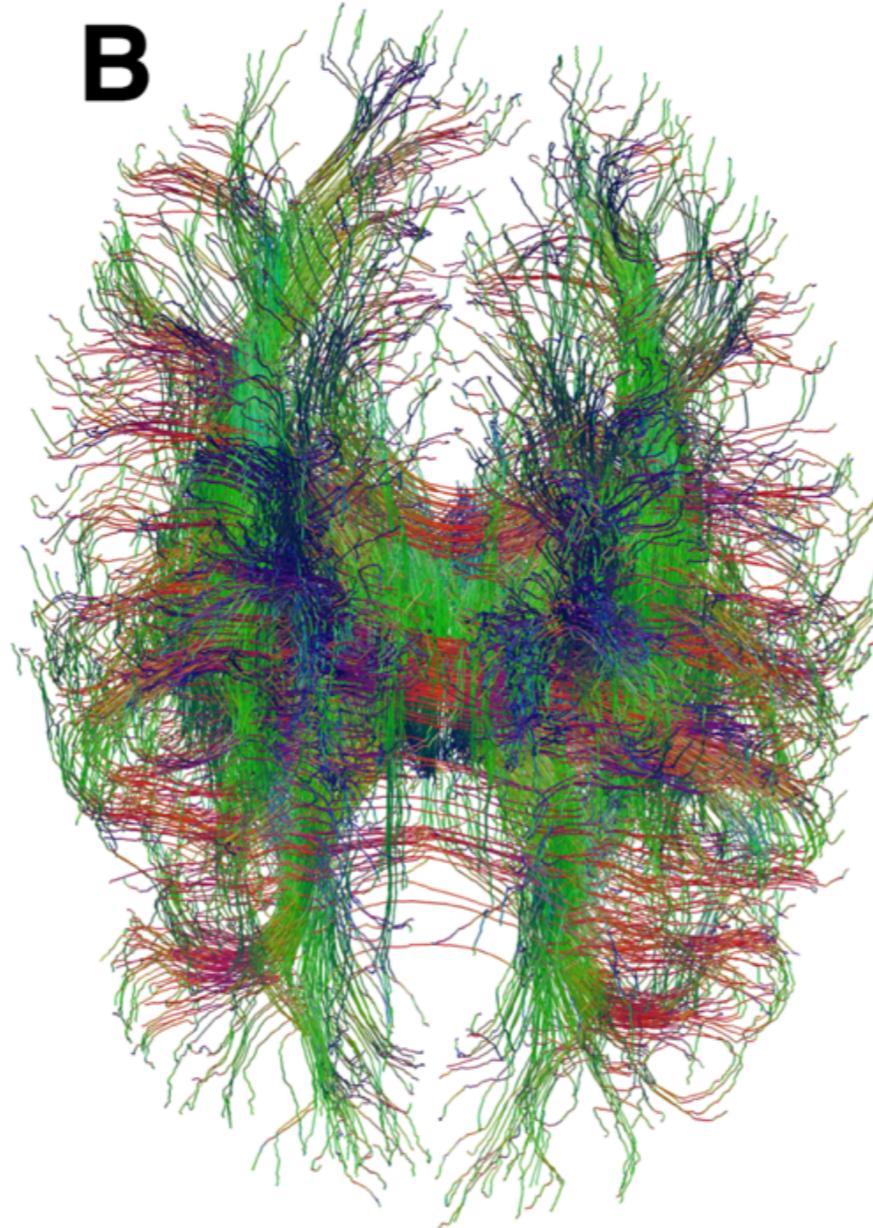
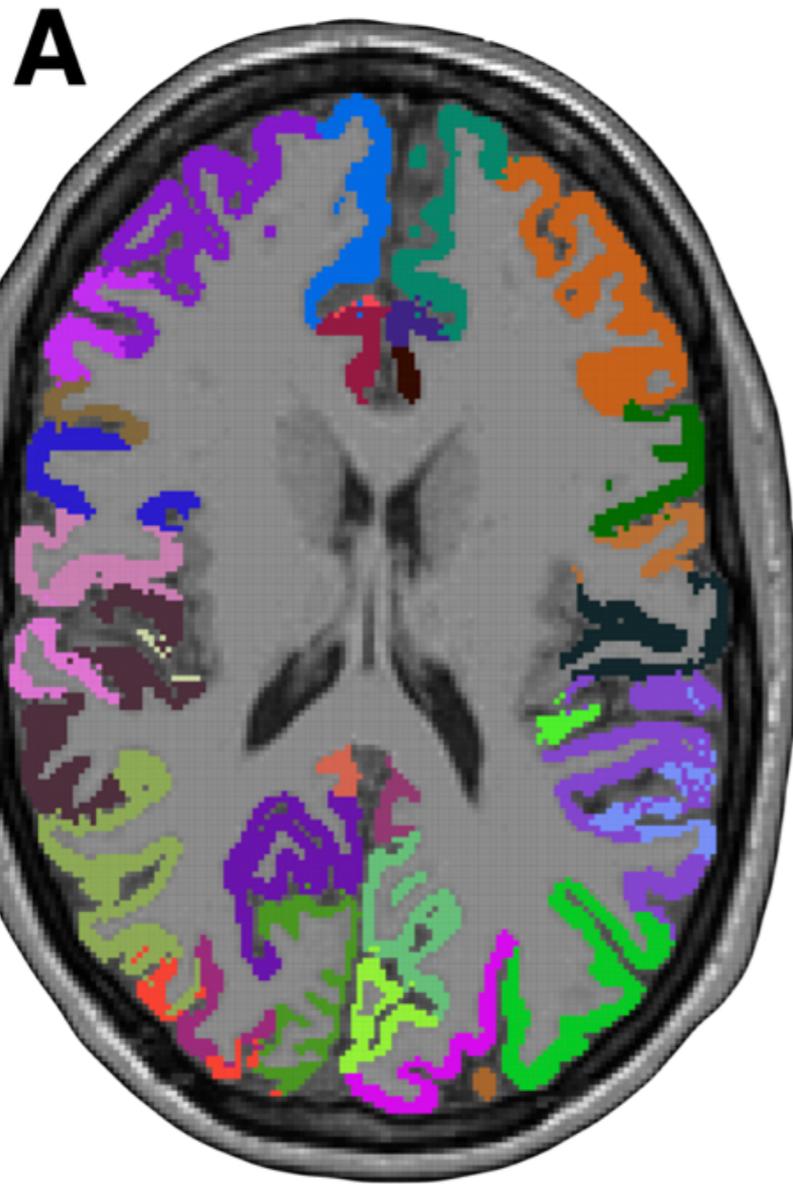
# Structural connectivity: tractography



## Functional connectivity: correlated time-courses



# *In vivo* connectomics



## Graph characteristics

- A range of measures have been developed in graph theory to describe characteristics of graphs and their vertices
- **Connection density**: the proportion of all possible edges which are present in the graph (cost)
- Average **path length**: the mean shortest path length between pairs of vertices (efficiency)
- **Betweenness centrality**: the number of shortest paths between other vertices which pass through a particular vertex (hubs)

## Clinical and cognitive relationships

- **Epilepsy** patients show increased path lengths in cortical thickness networks (Bernhardt et al., *Cereb Cortex*, 2011)
- Changes to hubs and clustering properties of networks based on grey matter volume in patients with **schizophrenia** (Bassett et al., *J Neurosci*, 2008)
- Path length in functional networks related to **intelligence** (Langer et al., *Hum Brain Mapp*, 2011)
- Tractography-based structural network efficiency related to cognitive abilities in **old age** (Wen et al., *J Neurosci*, 2011)

## Scope and limitations

- A graph can be created using any measure of association between brain regions of interest...
- ... but an association does not necessarily correspond to a direct connection
- Establishing direction of connections is challenging
- Abstract nature of graph makes systematic errors in underlying data invisible
- All the caveats of any preprocessing steps apply
- Choice of regions to use as vertices matters (cf. Zalesky et al., *NeuroImage*, 2010), but is usually arbitrary
- Substantial methodological variation in the literature

## Some questions

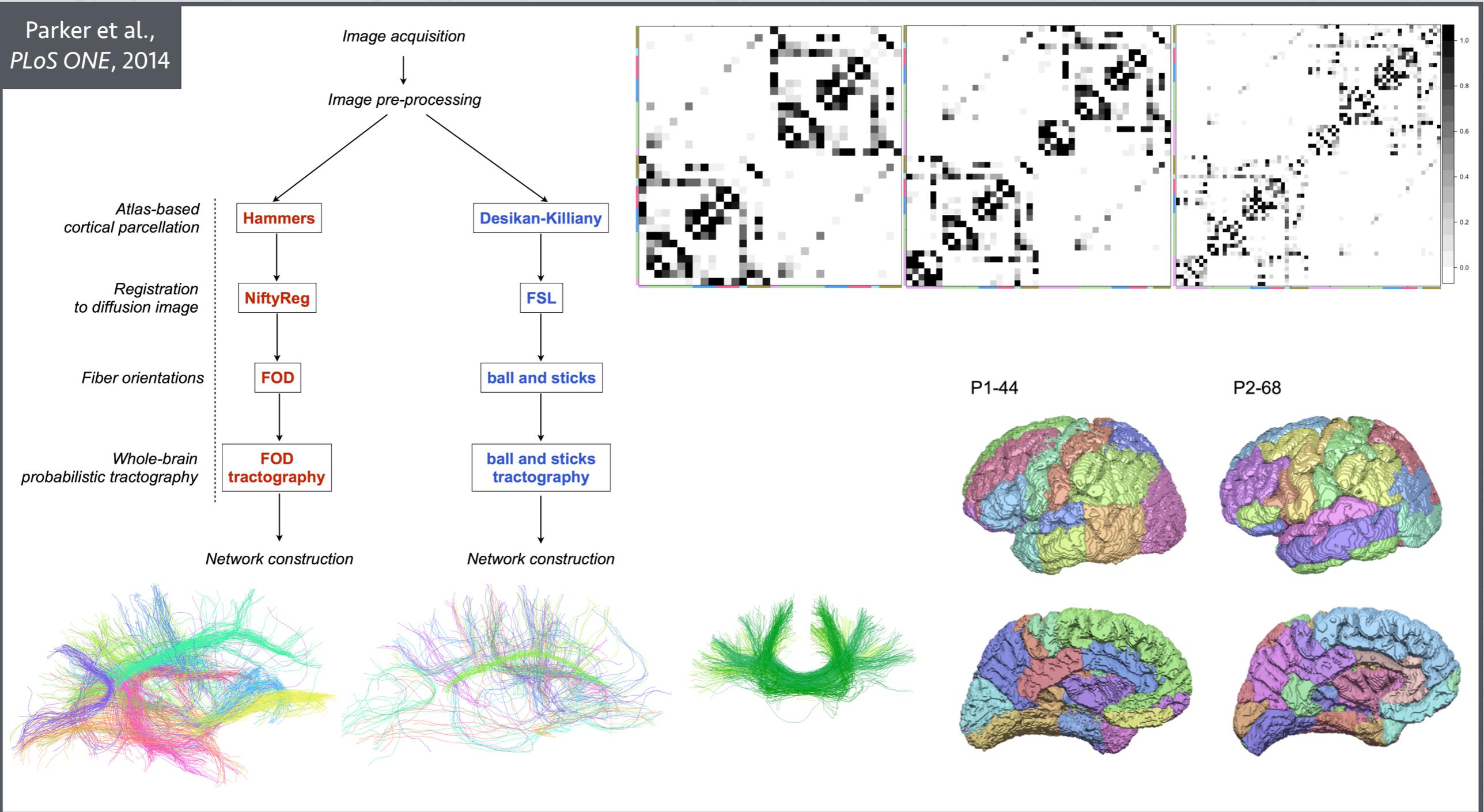
- How **robust** are reconstructed connectomes?
- How can one identify important **subnetworks** without strong prior expectations?
- To what extent does structure **predict** function?
- How should one **combine** information from different modalities?

## Robustness

- There is little consistency in the processes used to reconstruct connectomes
- Different pipelines may result in different results and therefore conclusions
- We need confidence in the robustness of the result if we want to make reliable scientific inferences

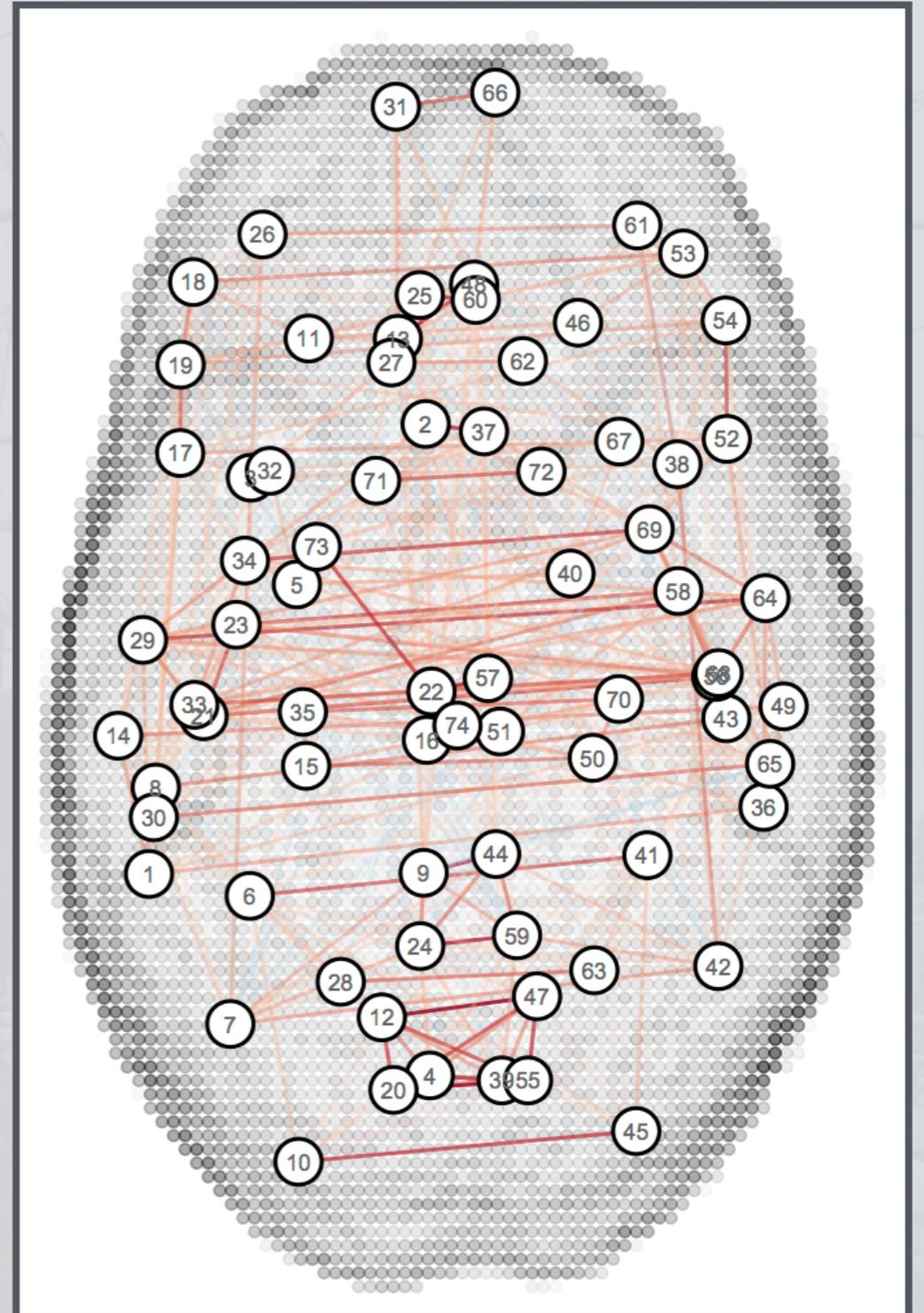
# Robust connections across data processing pipelines

Parker et al.,  
PLoS ONE, 2014

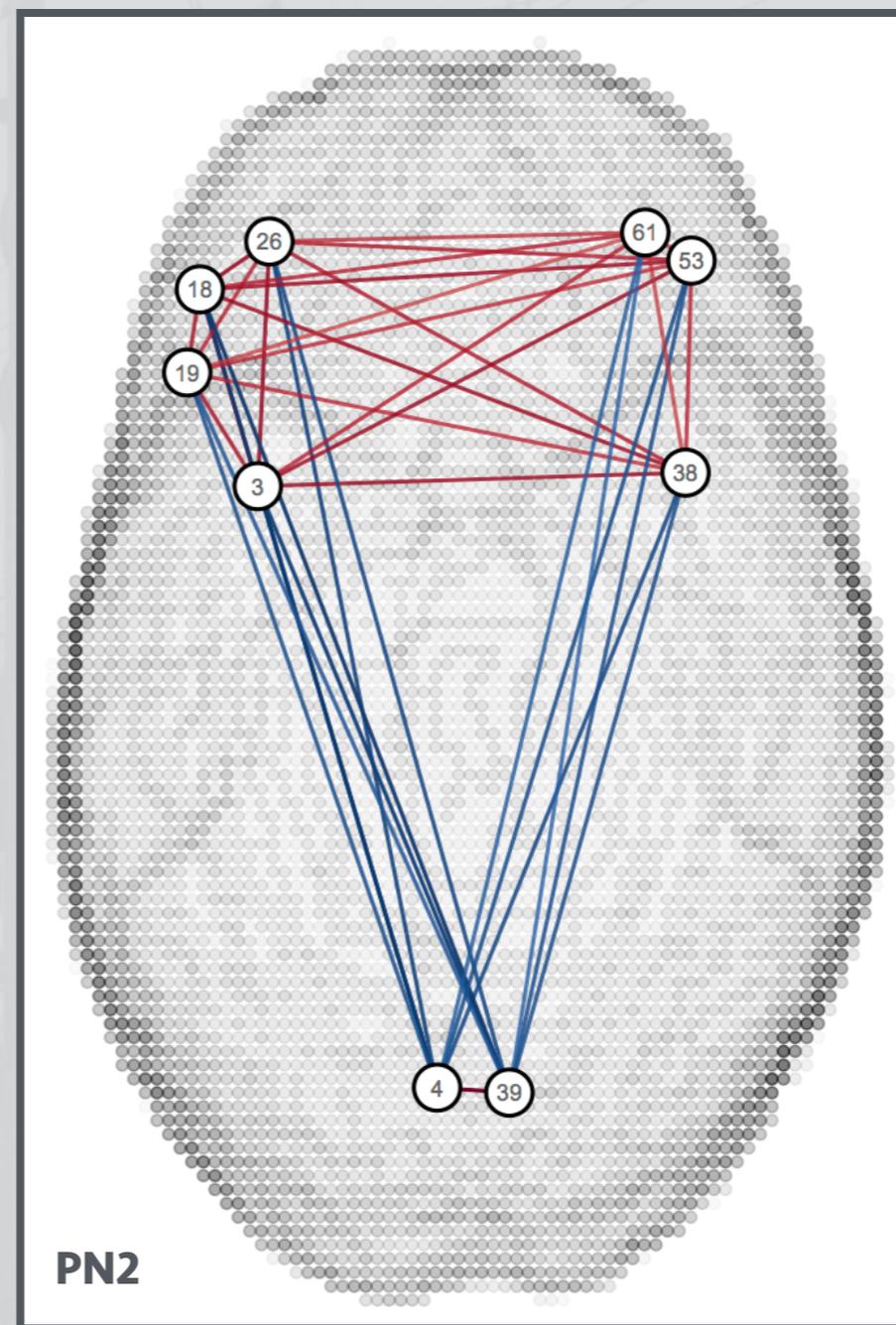
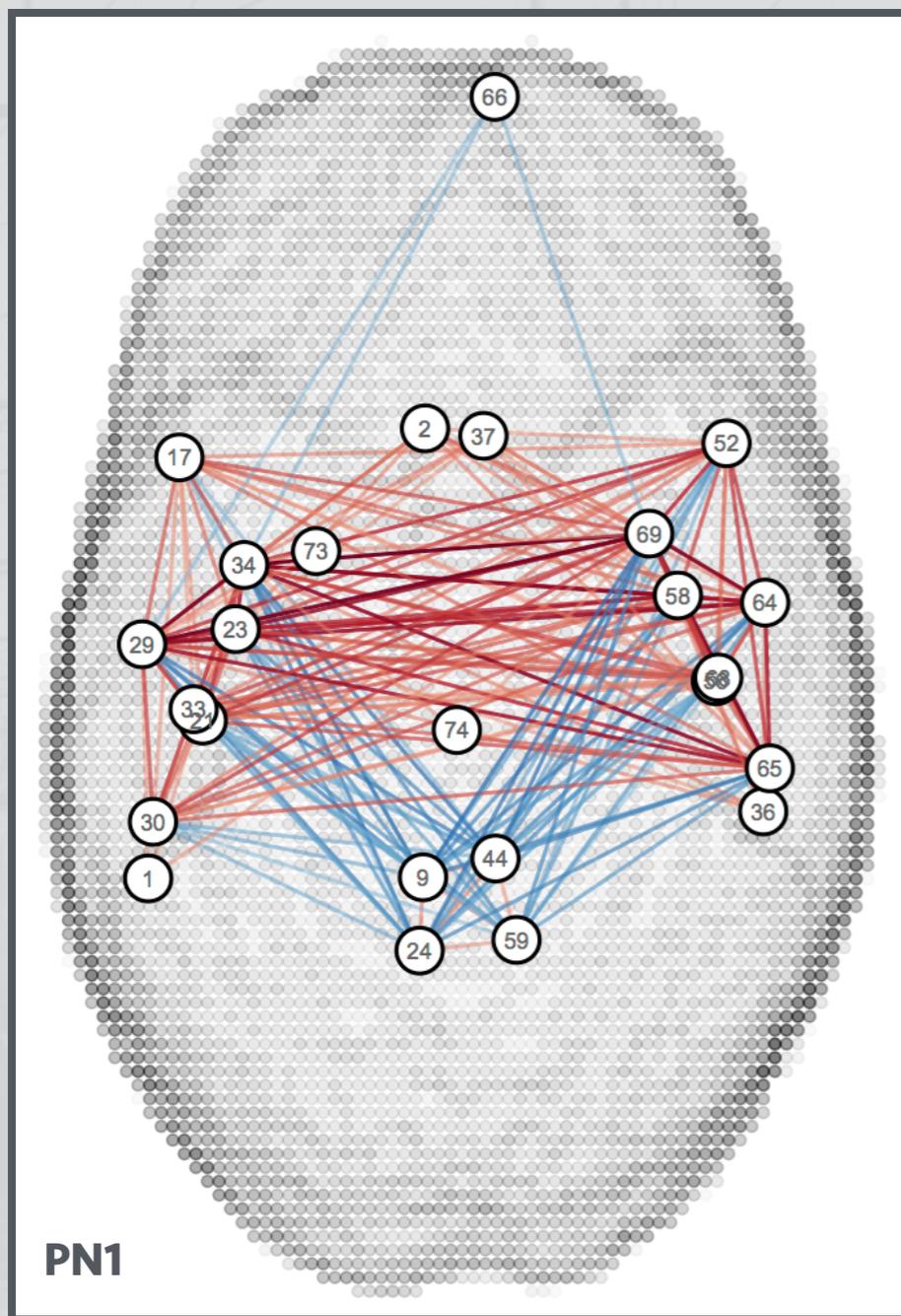


## The whole connectome?

- Connectome-level analysis is now becoming common
- Graph theory can be used to describe network topology
- But it is reasonable to assume that the whole network is not involved in any given task
- Therefore development and disease processes may not show up as global topology changes
- Strategy: **partition** or **decompose** network into interesting subnetworks



# Principal networks

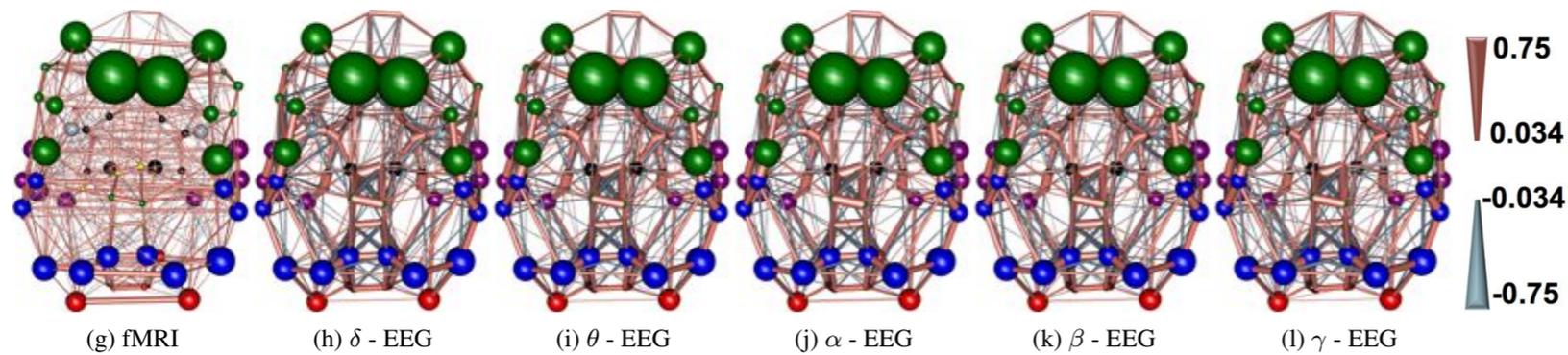


cf. Clayden et al., *PLoS ONE*, 2013

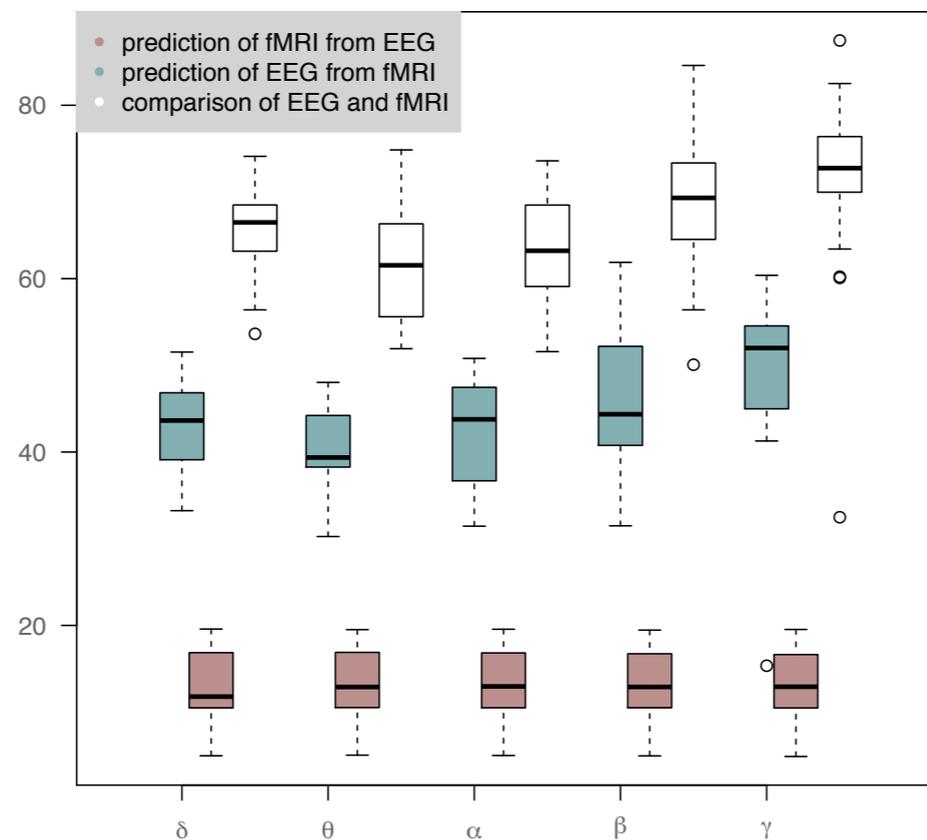
## Between-modality prediction

- Given a connectome from one modality, can we predict another?
- Are some measures of connectivity better than others for this purpose?
- What information is most useful for the prediction?

# Inter-modal functional connectivity



■ frontal ■ parietal ■ occipital ■ temporal ■ limbic ■ insula ■ sub-cortical



Deligianni et al., *Front Neurosci*, 2014

## Structural vs functional

- Structural and functional connectivity are conceptually different...
- ... but are underpinned by the same systems
- There should be substantial commonality
- Graph approaches allow the two to be represented similarly...
- ... but patterns of connectivity often differ in important ways
- Functional connectivity is often found to be more variable than structural connectivity
- Combining the two effectively remains an elusive goal for now

## Areas of current and future interest

- Joint **modelling** of structural and functional connectivity
- Characterisation of population **variability** in connectivity patterns
- Integration of **prior knowledge** into connectome analysis
- **Specialisation** of image analysis approaches for sensitivity in particular diseases
- One-versus-many approaches for identifying abnormalities in **individual patients**

# Thanks

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